CLAIMS

1. A method of estimating the colloidal stability of a preparation of compacted nucleic acids, comprising the steps of:

determining a turbidity parameter of a solution of compacted nucleic acid, wherein the turbidity parameter is defined as the slope of a straight line obtained by plotting log of apparent absorbance of light versus log of incident wavelength of the light, wherein said wavelength is between about 320 nm and 420 nm;

identifying the preparation as colloidally stable if a turbidity parameter of less than -3 is determined and identifying the preparation as colloidally unstable if a turbidity parameter of greater than or equal to -3 is determined.

2. A non-naturally occurring composition comprising unaggregated nucleic acid complexes, each complex consisting essentially of a single nucleic acid molecule and one or more polycation molecules, said polycation molecules having a counterion selected from the group consisting of acetate, bicarbonate, and chloride, wherein said complex is compacted to a diameter which is less than (a) double the theoretical diameter of a complex of said single nucleic acid molecule and a sufficient number of polycation molecules to provide a charge ratio of about 1:1, in the form of a condensed sphere, or (b) 30 nm, whichever is larger.

3. The composition of claim 2 wherein the polycation molecules are polylysine or a polylysine derivative.

4. The composition of claim 3 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

5. The composition of claim 2, said complex is compacted to a diameter of less than 90 nm.

6. The composition of claim 2, wherein the nucleic acid complex is compacted to a diameter less than 30 nm.

7. The composition of claim 2, wherein the nucleic acid complex is compacted to a diameter less than 23 nm.

8. The composition of claim 2, wherein the nucleic acid complex is compacted to a diameter not more than 12 nm.

9. The composition of claim 2 wherein said complex is compacted to a diameter which is less than double the theoretical diameter of a complex of said single nucleic acid and a sufficient number of positively charged residues to provide a charge ratio of about 1:1, in the form of a condensed sphere.

10. A method of preparing a composition according to claim 2 which comprises mixing the nucleic acid with the polycation having acetate as a counterion, at a salt concentration sufficient for compaction of the complex.

11. The method of claim 10 in which the mixing is monitored to detect, prevent or correct, the formation of aggregated or relaxed complexes.

12. The method of claim 10 wherein the salt is NaCl.

13. The method of claim 10 wherein the nucleic acid and the polycation are each, at the time of mixing, in a solution having a salt concentration of 0.05 to 1.5 M.

14. The method of claim 10 in which the molar ratio of the phosphate groups of the nucleic acid to the positively charged groups of the polycation is in the range of 4:1 to 1:4.

15. The method of claim 10 in which the polycation is added to the nucleic acid, while vortexing at high speed.

16. The method of claim 10 in which the nucleic acid is added to the polycation, while vortexing at high speed.

17. The method of claim 10 wherein the mixing is monitored by a method selected from the group consisting of electron microscopy, light scattering, circular dichroism, and absorbance measurement.

18. The method of claim 10 wherein the polycation molecules are polylysine or a polylysine derivative.

19. The method of claim 18 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

20. A non-naturally occurring composition comprising unaggregated nucleic acid complexes, each complex consisting essentially of a single nucleic acid molecule and one or more polycation molecules, wherein said polycation molecules have a counterion selected from the group consisting of acetate, bicarbonate, and chloride, said polycation molecule having a nucleic acid binding moiety through which it is complexed to the nucleic acid, wherein said nucleic acid molecule encodes at least one functional protein, wherein said complex is compacted to a diameter which is less than double the theoretical minimum diameter of a complex of said single nucleic acid molecule and a sufficient number of polycation molecules to provide a charge ratio of about 1:1, in the form of a condensed sphere, or 30 nm, whichever is larger.

21. The composition of claim 20 wherein the polycation molecules are polylysine or a polylysine derivative.

22. The composition of claim 21 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

23. The non-naturally occurring composition of claim 20 wherein said nucleic acid molecule comprises a promoter which controls transcription of an RNA molecule encoding the functional protein.

24. The non-naturally occurring composition of claim 20 wherein the protein is therapeutic.

25. The non-naturally occurring composition of claim 20 wherein the complex is compacted to a diameter which is less than 50 nm.

26. The non-naturally occurring composition of claim 20 wherein the complex is compacted to a diameter which is less than 30 nm.

27. The non-naturally occurring composition of claim 20 wherein the nucleic acid complex is compacted to a diameter less than 23 nm.

28. The non-naturally occurring composition of claim 20 wherein the nucleic acid complex is compacted to a diameter not more than 12 nm.

29. A non-naturally occurring composition comprising unaggregated nucleic acid complexes, each complex consisting essentially of a single double-stranded cDNA molecule and one or more polycation molecules, said polycation molecules having a counterion selected from the group consisting of acetate, bicarbonate, and chloride, wherein said cDNA molecule encodes at least one functional protein, wherein said complex is compacted to a diameter which is less than double the theoretical minimum diameter of a complex of said single cDNA molecule and a sufficient number of polycation molecules to provide a charge ratio of about 1:1, in the form of a condensed sphere, or 30 nm, whichever is larger.

30. The composition of claim 29 wherein the polycation molecules are polylysine or a polylysine derivative.

31. The composition of claim 30 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

32. A non-naturally occurring composition comprising unaggregated nucleic acid complexes, each complex consisting essentially of a single nucleic acid molecule and one or more polycation molecules, said polycation molecules having a counterion selected from the group consisting of acetate, bicarbonate, and chloride, wherein said nucleic acid molecule encodes at least one antisense nucleic acid, wherein said complex is compacted to a diameter which is less than double the theoretical minimum diameter of a complex of said single nucleic acid molecule and a sufficient number of polycation molecules to provide a charge ratio of about 1:1, in the form of a condensed sphere, or 30 nm, whichever is larger.

33. The composition of claim 32 wherein the polycation molecules are polylysine or a polylysine derivative.

34. The composition of claim 33 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

35. A non-naturally occurring composition comprising unaggregated nucleic acid complexes, each complex consisting essentially of a single nucleic acid molecule and one or more polycation molecules, said polycation molecule having a counterion selected from the group consisting of acetate, bicarbonate, and chloride, wherein said nucleic acid molecule is an RNA molecule, wherein said complex is compacted to a diameter which is less than double the theoretical minimum diameter of a complex of said single nucleic acid molecule and a sufficient number of polycation molecules to provide a charge ratio of about 1:1, in the form of a condensed sphere, or 30 nm, whichever is larger.

36. The composition of claim 35 wherein the polycation molecules are polylysine or a polylysine derivative.

37. The composition of claim 36 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

38. A method of preparing a composition comprising unaggregated nucleic acid complexes, each complex consisting essentially of a single nucleic acid molecule and one or more polycation molecules, said method comprising:

mixing a nucleic acid molecule with a polycation molecule at a salt concentration sufficient for compaction of the complex to a diameter which is less than double the theoretical minimum diameter of a complex of said single nucleic acid molecule and a sufficient number of polycation molecules to provide a charge ratio of about 1:1, in the form of a condensed sphere, or 30 nm, whichever is larger, whereby unaggregated nucleic acid complexes are formed, wherein each complex consists essentially of a single nucleic acid molecule and one or more polycation molecules, and wherein said polycation molecules have a counterion selected from the group consisting of bicarbonate and chloride.

39. The method of claim 38 wherein the polycation molecules are polylysine or a polylysine derivative.

40. The method of claim 39 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

41. A method of preparing a composition comprising unaggregated nucleic acid complexes, each complex consisting essentially of a single nucleic acid molecule and one or more polycation molecules, said method comprising:

mixing a nucleic acid molecule with a polycation molecule in a solvent to form a complex, said mixing being performed in the absence of added salt, whereby the nucleic acid forms soluble complexes with the polycation molecule without forming aggregates, wherein each complex consists essentially of a single nucleic acid molecule and one or more polycation molecules, wherein the complexes have a diameter which is less than double the theoretical minimum diameter of a complex of said single nucleic acid molecule and a sufficient number of polycation molecules to provide a charge ratio of

about 1:1, in the form of a condensed sphere, or 30 nm, whichever is larger, wherein the polycation has acetate as a counterion.

42. The method of claim 41 wherein the polycation molecules are polylysine or a polylysine derivative.

43. The method of claim 42 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

44. A method of preparing a composition comprising unaggregated nucleic acid complexes, each complex consisting essentially of a single nucleic acid molecule and one or more polycation molecules, said method comprising:

mixing a nucleic acid molecule with a polycation molecule in a solvent to form a complex, said mixing being performed in the absence of added salt, whereby the nucleic acid forms soluble complexes with the polycation molecule without forming aggregates, wherein each complex consists essentially of a single nucleic acid molecule and one or more polycation molecules, wherein the complexes have a diameter which is less than double the theoretical minimum diameter of a complex of said single nucleic acid molecule and a sufficient number of polycation molecules to provide a charge ratio of about 1:1, in the form of a condensed sphere, or 30 nm, whichever is larger, wherein the polycation has a counterion selected from the group consisting of bicarbonate and chloride.

45. The method of claim 44 wherein the polycation molecules are polylysine or a polylysine derivative.

46. The method of claim 45 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

47. Non-naturally occurring, soluble compacted complexes of a nucleic acid and a polycation molecule made by the process of claim 10.

48. Non-naturally occurring, soluble compacted complexes of a nucleic acid and a polycation molecule made by the process of claim 38.

49. Non-naturally occurring, soluble compacted complexes of a nucleic acid and a polycation molecule made by the process of claim 41.

50. Non-naturally occurring, soluble compacted complexes of a nucleic acid and a polycation made by the process of claim 44.

51. The complexes of claim 47 wherein the polycation molecules are polylysine or a polylysine derivative.

52. The complexes of claim 51 wherein the polylysine derivative is polylysine peptide with a cysteine residue

53. The complexes of claim 48 wherein the polycation molecules are polylysine or a polylysine derivative.

54. The complexes of claim 53 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

55. The complexes of claim 49 wherein the polycation molecules are polylysine or a polylysine derivative.

56. The complexes of claim 55 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

57. The complexes of claim 50 wherein the polycation molecules are polylysine or a polylysine derivative.

58. The complexes of claim 57 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

59. A method of preventing or treating a disease or other clinical condition in a subject which comprises:

administering intramuscularly or to the lung of the subject a prophylactically or therapeutically effective amount of a composition comprising:

unaggregated nucleic acid complexes, each complex consisting essentially of a single nucleic acid molecule and one or more polycation molecules, said polycation molecule having acetate as a counterion, wherein said complex is compacted to a diameter which is less than (a) double the theoretical minimum diameter of a complex of said single nucleic acid molecule and a sufficient number of polycation molecules to provide a charge ratio of about 1:1, in the form of a condensed sphere, or (b) 30 nm, whichever is larger,

said nucleic acid being one whose integration, hybridization or expression within target cells of said subject prevents or treats said disease or other clinical condition.

60. The method of claim 59 wherein the step of administering is by inhalation .

61. The method of claim 59 wherein the step of administering is by intramuscular injection.

62. The method of claim 59 wherein the polycation molecules are polylysine or a polylysine derivative.

63. The method of claim 62 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

64. A method of preventing or treating a disease or other clinical condition in a subject which comprises:

administering intramuscularly or to the lung of the subject a prophylactically or therapeutically effective amount of a composition comprising:

unaggregated nucleic acid complexes, each complex consisting

essentially of a single nucleic acid molecule and one or more

polycation molecules, said polycation molecule having a counterion selected from the group consisting of bicarbonate and chloride, wherein said complex is compacted to a diameter which is less than (a) double the theoretical minimum diameter of a complex of said single nucleic acid molecule and a sufficient number of polycation molecules to provide a charge ratio of about 1:1, in the form of a condensed sphere, or (b) 30 nm, whichever is larger,
said nucleic acid being one whose integration, hybridization or expression within target cells of said subject prevents or treats said disease or other clinical condition.

65. The method of claim 64 wherein the polycation molecules are polylysine or a polylysine derivative.

66. The method of claim 65 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

67. The method of claim 64 wherein the step of administering is by inhalation.

68. The method of claim 64 wherein the step of administering is by intramuscular injection.

69. The composition of claim 20 wherein said complex is compacted to a diameter which is less than double the theoretical diameter of a complex of said single nucleic acid and a sufficient number of positively charged residues to provide a charge ratio of about 1:1, in the form of a condensed sphere.

70. The composition of claim 29 wherein the nucleic acid complexes are associated with a lipid.

71. The composition of claim 29 wherein said complex is compacted to a diameter of less than 90 nm.

72. The composition of claim 29 wherein the nucleic acid complex is compacted to a diameter less than 30 nm.

73. The composition of claim 29 wherein the nucleic acid complex is compacted to a diameter less than 23 nm.

74. The composition of claim 29 wherein the nucleic acid complex is compacted to a diameter not more than 12 nm.

75. The composition of claim 29 wherein said complex is compacted to a diameter which is less than double the theoretical diameter of a complex of said single nucleic acid and a sufficient number of positively charged residues to provide a charge ratio of about 1:1, in the form of a condensed sphere.

76. The composition of claim 32 wherein said complex is compacted to a diameter of less than 90 nm.

77. The composition of claim 32 wherein the nucleic acid complex is compacted to a diameter less than 30 nm.

78. The composition of claim 32 wherein the nucleic acid complex is compacted to a diameter less than 23 nm.

79. The composition of claim 32 wherein the nucleic acid complex is compacted to a diameter not more than 12 nm.

80. The composition of claim 32 wherein said complex is compacted to a diameter which is less than double the theoretical diameter of a complex of said single nucleic acid and a sufficient number of positively charged residues to provide a charge ratio of about 1:1, in the form of a condensed sphere.

81. The composition of claim 35 said complex is compacted to a diameter of less than 90 nm.

82. The composition of claim 35 wherein the nucleic acid complex is compacted to a diameter less than 30 nm.

83. The composition of claim 35 wherein the nucleic acid complex is compacted to a diameter less than 23 nm.

84. The composition of claim 35 wherein the nucleic acid complex is compacted to a diameter not more than 12 nm.

85. The composition of claim 35 wherein said complex is compacted to a diameter which is less than double the theoretical diameter of a complex of said single nucleic acid and a sufficient number of positively charged residues to provide a charge ratio of about 1:1, in the form of a condensed sphere.

86. The method of claim 38 wherein the salt is NaCl.

87. The method of claim 38 wherein the nucleic acid and the polycation are each, at the time of mixing, in a solution having a salt concentration of 0.05 to 1.5 M.

88. The method of claim 38 in which the mixing is monitored to detect, prevent or correct, the formation of aggregated or relaxed complexes.

89. The method of claim 38 in which the molar ratio of the phosphate groups of the nucleic acid to the positively charged groups of the polycation is in the range of 4:1 to 1:4.

90. The method of claim 38 in which the polycation is added to the nucleic acid, while vortexing at high speed.

91. The method of claim 38 in which the nucleic acid is added to the polycation, while vortexing at high speed.

92. The method of claim 38 wherein the mixing is monitored by a method selected from the group consisting of electron microscopy, light scattering, circular dichroism, and absorbance measurement.

93. The method of claim 41 in which the mixing is monitored to detect, prevent or correct, the formation of aggregated or relaxed complexes.

94. The method of claim 41 in which the molar ratio of the phosphate groups of the nucleic acid to the positively charged groups of the polycation is in the range of 4:1 to 1:4.

95. The method of claim 41 in which the polycation is added to the nucleic acid, while vortexing at high speed.

96. The method of claim 41 in which the nucleic acid is added to the polycation, while vortexing at high speed.

97. The method of claim 41 wherein the mixing is monitored by a method selected from the group consisting of electron microscopy, light scattering, circular dichroism, and absorbance measurement.

98. The method of claim 44 in which the mixing is monitored to detect, prevent or correct, the formation of aggregated or relaxed complexes.

99. The method of claim 44 in which the molar ratio of the phosphate groups of the nucleic acid to the positively charged groups of the polycation is in the range of 4:1 to 1:4.

100. The method of claim 44 in which the polycation is added to the nucleic acid, while vortexing at high speed.

101. The method of claim 44 in which the nucleic acid is added to the polycation, while vortexing at high speed.

102. The method of claim 44 wherein the mixing is monitored by a method selected from the group consisting of electron microscopy, light scattering, circular dichroism, and absorbance measurement.

103. A non-naturally occurring composition comprising unaggregated nucleic acid complexes, each complex consisting essentially of a single nucleic acid molecule and one or more polycation molecules, said polycation molecules having a counterion selected from the group consisting of acetate, bicarbonate, and chloride.

104. The composition of claim 103 wherein the counterion is acetate.

105. The composition of claim 2 wherein said polycation is CK15-60P10 and the counterion is acetate, wherein CK15-60P10 is a polyamino acid polymer of one N-terminal cysteine and 15-60 lysine residues, wherein a molecule of polyethylene glycol having an average molecular weight of 10 kdal is attached to the cysteine residue.

106. The composition of claim 105 wherein the polycation molecule comprises 30 residues of lysine.

107. The composition of claim 105 wherein the polycation molecule comprises a targeting moiety.

108. The composition of claim 105, said complex is compacted to a diameter of less than 90 nm.

109. The composition of claim 105, wherein the nucleic acid complex is compacted to a diameter less than 30 nm.

110. The composition of claim 105, wherein the nucleic acid complex is compacted to a diameter less than 23 nm.

111. The composition of claim 105, wherein the nucleic acid complex is compacted to a diameter not more than 12 nm.

112. The composition of claim 105 wherein said complex is compacted to a diameter which is less than double the theoretical diameter of a complex of said single nucleic acid and a sufficient number of positively charged residues to provide a charge ratio of about 1:1, in the form of a condensed sphere.

113. The composition of claim 105 which is lyophilized.

114. The composition of claim 105 which is rehydrated after lyophilization.

115. The composition of claim 105 which does not contain a disaccharide.

116. A method of delivering polynucleotides to cells comprising:

contacting the composition of claim 114 with cells, whereby the nucleic acid is delivered to and taken up by the cells.

117. The method of claim 116 wherein the composition does not contain a disaccharide.

118. The composition of claim 20 wherein the polycation is CK15-60P10, and the counterion is acetate, wherein CK15-60 is a polyamino acid polymer of one N-terminal cysteine and 15-60 lysine residues, wherein a molecule of polyethylene glycol having an average molecular weight of 10 kdal is attached to the cysteine residue.

119. The composition of claim 118 wherein the polycation molecule comprises 30 residues of lysine.

120. The composition of claim 118 wherein the polycation molecule comprises a targeting moiety.

121. The composition of claim 118 which is lyophilized.

122. The non-naturally occurring composition of claim 118 wherein said nucleic acid molecule comprises a promoter which controls transcription of an RNA molecule encoding the functional protein.

123. The non-naturally occurring composition of claim 118 wherein the protein is therapeutic.

124. The non-naturally occurring composition of claim 118 wherein the complex is compacted to a diameter which is less than 50 nm.

125. The non-naturally occurring composition of claim 118 wherein the complex is compacted to a diameter which is less than 30 nm.

126. The non-naturally occurring composition of claim 118 wherein the nucleic acid complex is compacted to a diameter less than 23 nm.

127. The non-naturally occurring composition of claim 118 wherein the nucleic acid complex is compacted to a diameter not more than 12 nm.

128. The composition of claim 118 wherein said complex is compacted to a diameter which is less than double the theoretical diameter of a complex of said single nucleic acid and a sufficient number of positively charged residues to provide a charge ratio of about 1:1, in the form of a condensed sphere.

129. The composition of claim 118 which is rehydrated after lyophilization.

130. The composition of claim 118 which does not contain a disaccharide.

131. A method of delivering polynucleotides to cells comprising:

contacting the composition of claim 129 with cells, wherein the polynucleotide encodes a protein, whereby the protein is expressed.

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132. The composition of claim 29 wherein said polycation is CK15-60P10, and said counterion is acetate, wherein CK15-60P10 is a polyamino acid polymer of one N-terminal cysteine and 15-60 lysine residues, wherein a molecule of polyethylene glycol having an average molecular weight of 10 kdal is attached to the cysteine residue.

133. The composition of claim 132 wherein the polycation molecule comprises 30 residues of lysine.

134. The composition of claim 132 wherein the polycation molecule comprises a targeting moiety.

135. The composition of claim 132 which is lyophilized.

136. The composition of claim 132 wherein said complex is compacted to a diameter which is less than double the theoretical diameter of a complex of said single nucleic acid and a sufficient number of positively charged residues to provide a charge ratio of about 1:1, in the form of a condensed sphere.

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137. The composition of claim 132 which is rehydrated after lyophilization.

138. The composition of claim 132 which does not contain a disaccharide.

139. A method of delivering polynucleotides to cells comprising:

contacting the composition of claim 137 with cells, wherein the polynucleotide encodes a protein, whereby the protein is expressed.

140. The composition of claim 32 wherein said polycation is CK15-60P10, and the counterion is acetate, wherein CK15-60P10 is a polyamino acid polymer of one N-terminal cysteine and 15-60 lysine residues, wherein a molecule of polyethylene glycol having an average molecular weight of 10 kdal is attached to the cysteine residue.

141. The composition of claim 140 wherein the polycation molecule comprises 30 residues of lysine.

142. The composition of claim 140 wherein the polycation molecule comprises a targeting moiety.

143. The composition of claim 140 which is lyophilized.

144. The composition of claim 140 wherein said complex is compacted to a diameter which is less than double the theoretical diameter of a complex of said single nucleic acid and a sufficient number of positively charged residues to provide a charge ratio of about 1:1, in the form of a condensed sphere.

145. The composition of claim 140 which is rehydrated after lyophilization.

146. The composition of claim 140 which does not contain a disaccharide.

147. A method of delivering polynucleotides to cells comprising:

contacting the compositions of claim 145 with cells, wherein the polynucleotide encodes an antisense nucleic acid, whereby the antisense nucleic acid is expressed.

148. The composition of claim 35 wherein said polycation is CK15-60P10, and said counterion is acetate, wherein CK15-60P10 is a polyamino acid polymer of one N-

terminal cysteine and 15-60 lysine residues, wherein a molecule of polyethylene glycol having an average molecular weight of 10 kdal is attached to the cysteine residue.

149. The composition of claim 148 wherein the polycation molecule comprises 30 residues of lysine.

150. The composition of claim 148 wherein the polycation molecule comprises a targeting moiety.

151. The composition of claim 148 which is lyophilized.

152. The composition of claim 148 which is lyophilized and rehydrated.

153. The composition of claim 148 which does not contain a disaccharide.

154. A method of delivering polynucleotides to cells comprising:

contacting the composition of claim 152 with cells, whereby the polynucleotide is delivered to and taken up by the cells.

155. The method of claim 41, wherein said polycation is CK15-60P10, and said counterion is acetate, wherein CK15-60P10 is a polyamino acid polymer of one N-terminal cysteine and 15-60 lysine residues, wherein a molecule of polyethylene glycol having an average molecular weight of 10 kdal is attached to the cysteine residue.

156. The method of claim 155 further comprising lyophilizing the unaggregated nucleic acid complexes.

157. The method of claim 156 further comprising rehydrating the lyophilized nucleic acid complexes.

158. The method of claim 155 wherein the polycation molecule comprises 30 residues of lysine.

159. The method of claim 155 wherein the polycation molecule comprises a targeting moiety.

160. A method of preparing a composition comprising unaggregated nucleic acid complexes, each complex consisting essentially of a single nucleic acid molecule and one or more polycation molecules, said method comprising:

mixing a nucleic acid molecule with a polycation molecule at a salt concentration sufficient for compaction of the complex to a diameter which is less than double the theoretical minimum diameter of a complex of said single nucleic acid molecule and a sufficient number of polycation molecules to provide a charge ratio of about 1:1, in the form of a condensed sphere, or 30 nm, whichever is larger, whereby unaggregated nucleic acid complexes are formed, wherein each complex consists essentially of a single nucleic acid molecule and one or more polycation molecules, and wherein said polycation molecules have a counterion selected from the group consisting of acetate, bicarbonate and chloride.

161. The method of claim 160 wherein the counterion is acetate.

162. The method of claim 160 wherein the polycation molecules are polylysine or a polylysine derivative.

163. The method of claim 162 wherein the polylysine derivative is polylysine peptide with a cysteine residue.

164. Non-naturally occurring, soluble compacted complexes of a nucleic acid and a polycation molecule made by the method of claim 160.

165. The method of claim 160 wherein the salt is NaCl.

166. The method of claim 160 wherein the nucleic acid and the polycation are each, at the time of mixing, in a solution having a salt concentration of 0.05 to 1.5 M.

167. The method of claim 160 in which the mixing is monitored to detect, prevent or correct, the formation of aggregated or relaxed complexes.

168. The method of claim 160 in which the molar ratio of the phosphate groups of the nucleic acid to the positively charged groups of the polycation is in the range of 4:1 to 1:4.

169. The method of claim 160 in which the polycation is added to the nucleic acid, while vortexing at high speed.

170. The method of claim 160 in which the nucleic acid is added to the polycation, while vortexing at high speed.

171. The method of claim 160 wherein the mixing is monitored by a method selected from the group consisting of electron microscopy, light scattering, circular diochroism, and absorbance measurement.

172. The method of claim 160, wherein said polycation is CK15-60P10 and the counterion is acetate, wherein CK15-60P10 is a polyamino acid polymer of one N-terminal cysteine and 15-60 lysine residues, wherein a molecule of polyethylene glycol having an average molecular weight of 10 kdal is attached to the cysteine residue.

173. The method of claim 172 further comprising lyophilizing the unaggregated nucleic acid complexes.

174. The method of claim 173 further comprising rehydrating the lyophilized nucleic acid complexes.

175. The method of claim 172 wherein the polycation molecule comprises 30 residues of lysine.

176. The method of claim 172 wherein the polycation molecule comprises a targeting moiety.

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